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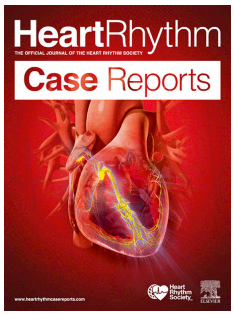

Torsades de Pointes Following Vaccination for COVID-19

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Torsades following COVID-19 vaccination

Key words: COVID, syncope, torsades de pointes, cardiac arrest, left bundle branch block

Introduction

Torsades de Pointes is a polymorphic ventricular tachycardia that can cause syncope and lead to sudden cardiac death. This arrhythmia is initiated by early after depolarizations in the setting of prolonged ventricular repolarization, manifesting as QT prolongation on the 12-lead electrocardiogram.[1] Common risk factors include QT prolonging medications, electrolyte disturbances, bradycardia, and certain inherited genetic mutations.[2] We report a case of Torsades de Pointes that occurred shortly after vaccination for COVID-19.

Case Report

A 65 year-old female with history of hypertension and left bundle branch block was referred to the Electrophysiology Clinic following a single episode of syncope. The episode occurred suddenly while sitting and was preceded by transient lightheadedness but without palpitations. An ECG at that time demonstrated sinus rhythm with left bundle branch block, premature atrial complexes, and premature ventricular complexes at a heart rate of 78 beats per minute (QRS 164 msec, QT 454 msec, QTc 517 msec, JT 290 msec) (Figure 1A). An echocardiogram demonstrated a left ventricular ejection fraction of 45-50% with left ventricular dyssynchrony and normal left ventricular wall thickness. The patient had previously completed her two-dose vaccination series for the Pfizer-BioNTech COVID-19 vaccine, having received the second dose one month before her syncopal episode.

She underwent a diagnostic electrophysiology study, which demonstrated normal sinus node function, normal AV node function, and mildly abnormal His-Purkinje system conduction

with negative procainamide challenge (HV interval 65 msec at baseline, prolonged to 73 msec following procainamide 10 mg/kg/min IV infusion over 10 minutes). After completing the procainamide of infusion, her QRS duration increased from 160 msec at baseline to 170 msec, her QTc increased from 525 msec at baseline to 630 msec, and her JT interval increased from 330 msec to 390 msec. Additionally, ventricular tachycardia was not inducible following programmed ventricular stimulation with 3 premature extrastimuli decremented to ventricular refractoriness at two drive train cycle lengths (600 ms and 400 ms) from the right ventricular apex. She ultimately received an implantable loop recorder.

Five months later, she received a third “booster” COVID-19 vaccination (Pfizer-BioNTech). Within 12 hours of receiving the vaccine, she suddenly became unresponsive while watching television. When she did not regain consciousness, her husband began cardiopulmonary resuscitation and contacted Emergency Medical Services. After paramedics arrived, application of an automated external defibrillator demonstrated ventricular fibrillation. Over the course of resuscitative efforts, she received 14 defibrillations.

Subsequent interrogation of her loop recorder demonstrated Torsades de Pointes (Figure 2A) with degeneration into ventricular fibrillation (Figure 2B). Her presenting ECG demonstrated an accelerated idioventricular rhythm at a heart rate of 79 beats per minute (Figure 1B). A repeat ECG soon after demonstrated sinus rhythm with left bundle branch block at a heart rate of 72 beats per minute (QRS 160 msec, QT 540 msec, QTc 592 msec, JT 380 msec) (Figure 3A). Due to the extensive burden of ventricular fibrillation during the cardiac arrest, amiodarone intravenous infusion was initiated.

She was intubated and subsequently underwent coronary angiography which demonstrated normal coronary arteries. Her initial high sensitivity Troponin I level was 30 ng/L, which rose to 18,697 ng/L 10 hours later. Her presenting serum chemistry demonstrated normal magnesium level of 2.4 mg/dL, a mildly low calcium level of 8.4 mg/dL, and a normal potassium level of 3.9 mmol/L. A repeat potassium level 3 hours later was 2.7 mmol/L which was replenished intravenously. A rapid COVID-19 PCR test was negative on admission. Her initial echocardiogram showed a reduced ejection fraction of 19%, which later normalized to 50% after starting metoprolol succinate. She underwent targeted temperature management for 48 hours (temperature 33.2 degrees Celsius) to preserve brain function. Subsequent ECGs demonstrated progressive QT prolongation with a maximum QTc of 705 msec (Figure 3B).

Junctional rhythm subsequently occurred, prompting discontinuation of amiodarone and temporary initiation of epinephrine infusion to improve chronotropy. A brain MRI demonstrated anoxic brain injury. Her hospitalization was further complicated by the development of ventilator-associated pneumonia with Serratia marcescens treated with intravenous piperacillin/tazobactam followed by a catheter-associated urinary tract infection with Candida albicans treated with oral fluconazole with close ECG monitoring. Following extubation, her neurologic function gradually returned. She underwent dual chamber implantable cardioverter defibrillator implantation with loop recorder explantation and successful defibrillator threshold testing. She was then discharged to a rehabilitation facility 7 weeks after admission.

Discussion

The cause of this patient's cardiac arrest is not completely understood. The ventricular arrhythmia recorded on the implantable loop recorder appears to be a polymorphic ventricular tachycardia with a twisting of points around a central axis consistent with Torsades de Pointes that rapidly degenerates into ventricular fibrillation. The QT interval on presentation was significantly prolonged compared to baseline, even when accounting for the left bundle branch block. However, this case was unusual as it was not preceded by a pause-dependency which typically initiates this arrhythmia.

An alternative explanation for the observed arrhythmia is ventricular fibrillation induced by a premature ventricular complex in context of a mild non-ischemic cardiomyopathy. This could explain why the QT interval does not appear to be significantly prolonged on the loop recorder rhythm strip in Figure 2A. However, the QT interval at this precordial location may not necessarily appear prolonged owing to regional differences in the QT interval between leads on a 12-lead ECG.[3] The presence of premature ventricular complexes on the presenting ECG in Figure 1 also supports this arrhythmia mechanism following her initial syncopal episode prior to loop recorder implantation. The presence of myocarditis, which has been linked to the COVID-19 vaccine by Pfizer-BioNTech[4], may have also increased the risk of arrhythmogenesis. Unfortunately, detailed cardiac imaging with PET or MRI were not performed as they were unavailable at the treating facility.

Following resuscitation from the cardiac arrest, our patient's presenting electrolytes demonstrated mild hypocalcemia, however serum potassium and magnesium levels were within normal limits; it was not until 3 hours following her initial presentation that she became profoundly hypokalemic as would be expected from a prolonged cardiac arrest. The mechanism

is thought to be from a transmembrane shift in potassium from the vascular space into cells caused by either a neurohumoral response to the cardiac arrest itself, catecholamine therapy during the arrest, or due to rapid correction of metabolic acidosis from the administration of bicarbonate and mechanical ventilation.[5,6]

The observed QT prolongation on subsequent ECGs could have been attributed to amiodarone and hypokalemia. The larger differences in the QT interval on different leads in Figure 3B (e.g. lead II compared to V2) suggest an elevated QT dispersion which is also associated with an increased risk of ventricular arrhythmias.[3] The presence of an inherited channelopathy such as Long QT Syndrome was considered. She had no history of syncope as a child and there was no significant family history. Genetic testing was not performed. New onset Torsades de Pointes in congenital Long QT Syndrome is rare starting at this age.

Given that her cardiac arrest occurred within 12 hours after receiving her COVID-19 vaccination, the vaccine itself should be considered as a potential contributor in a susceptible individual. However, it is also important to note that she did not report any significant side effects after receiving the first two doses of the same COVID-19 vaccine. Her single syncopal episode one month after receiving the second dose of the Pfizer-BioNTech COVID-19 vaccine may or may not have been related to the vaccine. It is possible that a non-sustained ventricular arrhythmia triggered by myocarditis could have caused her syncopal episode one month after the second vaccination, especially given the finding of a mildly reduced ejection fraction on her initial echocardiogram.

Vaccination against COVID-19 has been shown to reduce the incidence of severe illness, hospitalization, and death due to the virus and is associated with a low risk of adverse events.[7]

The Centers for Disease Control have recommended a booster vaccination for COVID-19 due to waning immunity several months following an initial vaccination series.[8] Although Torsades de Pointes is not a known side effect of COVID-19 vaccination, infection with SARS-CoV-2 has been associated with QT prolongation.[9] This finding has been attributed to excessive inflammation modulating potassium and calcium channels that can lead to ventricular arrhythmias including Torsades de Pointes. An excessive immune response following vaccination to COVID-19 may have contributed to our patient's cardiac arrest via a similar mechanism to that seen in patients during active COVID-19 infection.

Conclusions

This is the first known case of polymorphic ventricular tachycardia in the setting of QT prolongation following COVID-19 vaccination. Whether this was an episode of Torsades de Pointes or ventricular fibrillation triggered by a premature ventricular complex is open for debate. While this case does not prove a definitive causal link to the vaccine, continued data collection and adverse event reporting following vaccination is paramount to ensure safety of widespread vaccinations for the novel coronavirus.

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Figures:

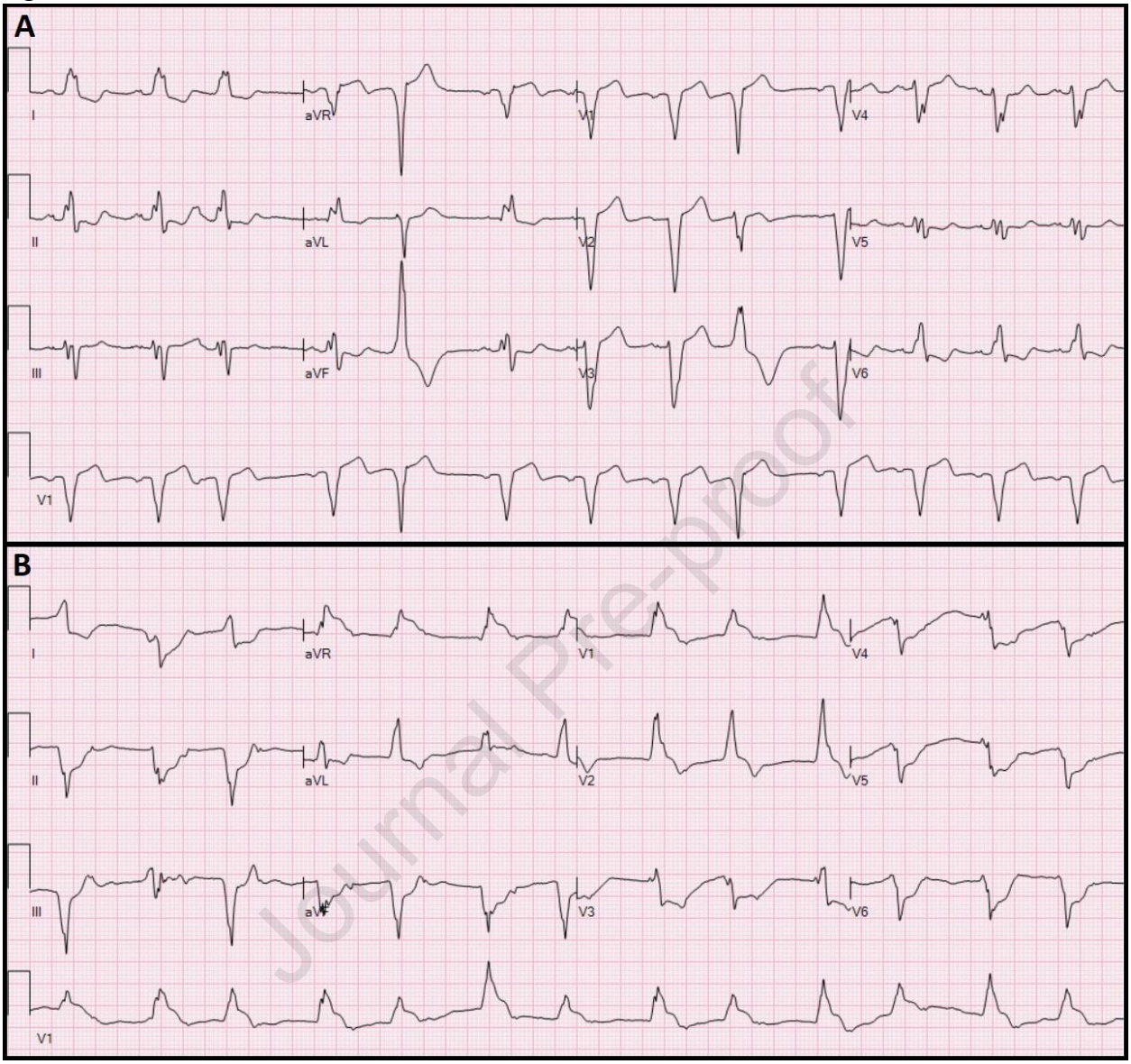

Figure 1. Panel A. Presenting ECG following the first episode of syncope. Heart rate 78 bpm, QRS 164 msec, QT 454 msec, QTc 517 msec, JT 290 msec. Panel B. Presenting ECG following cardiac arrest demonstrating an idioventricular rhythm at a heart rate of 79 beats per minute.

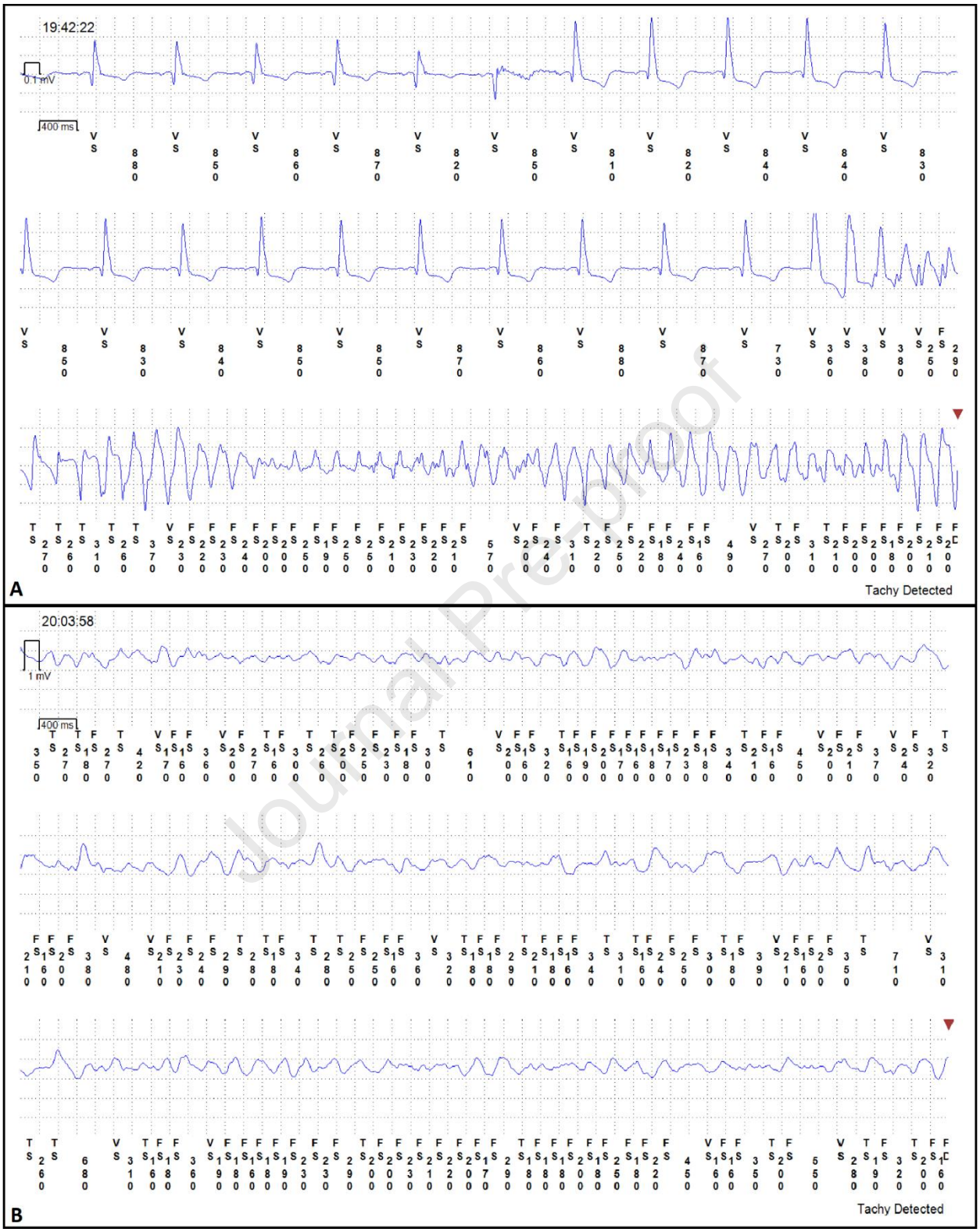

Figure 2. Panel A. Presenting rhythm on implantable loop recorder showing initiation of Torsades de Pointes. Panel B. Rhythm on implantable loop recorder several minutes later showing ventricular fibrillation.

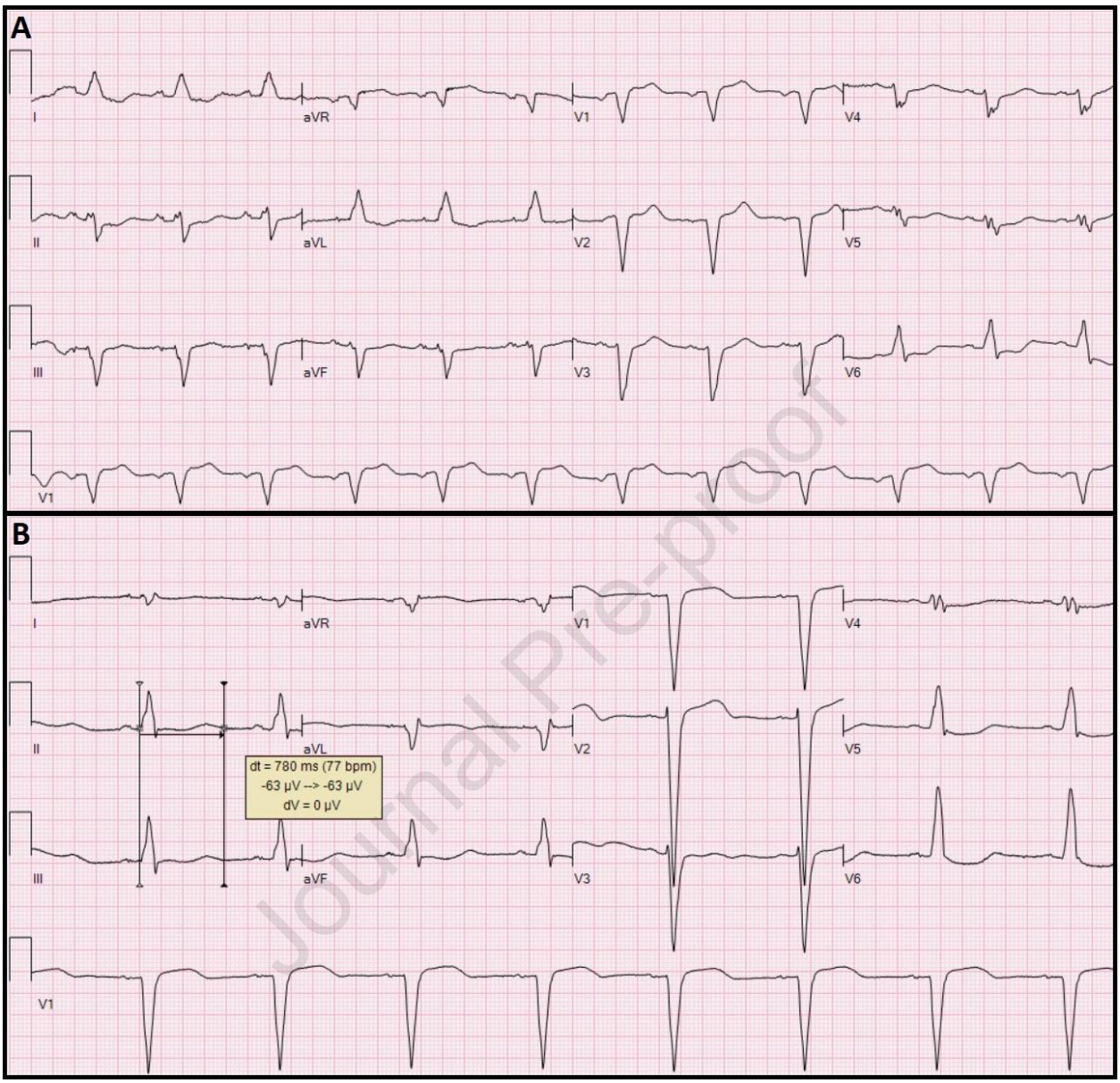

Figure 3. Panel A. Repeat ECG showing sinus rhythm with left bundle branch block at a heart rate of 72 beats per minute. QRS 160 msec, QT 540 msec, QTc 592 msec, JT 380 msec. Panel B. ECG while on amiodarone infusion showing sinus bradycardia at a heart rate of 49 beats per minute. QRS 170 msec, QT 780 msec, QTc 705 msec, JT 610 msec.

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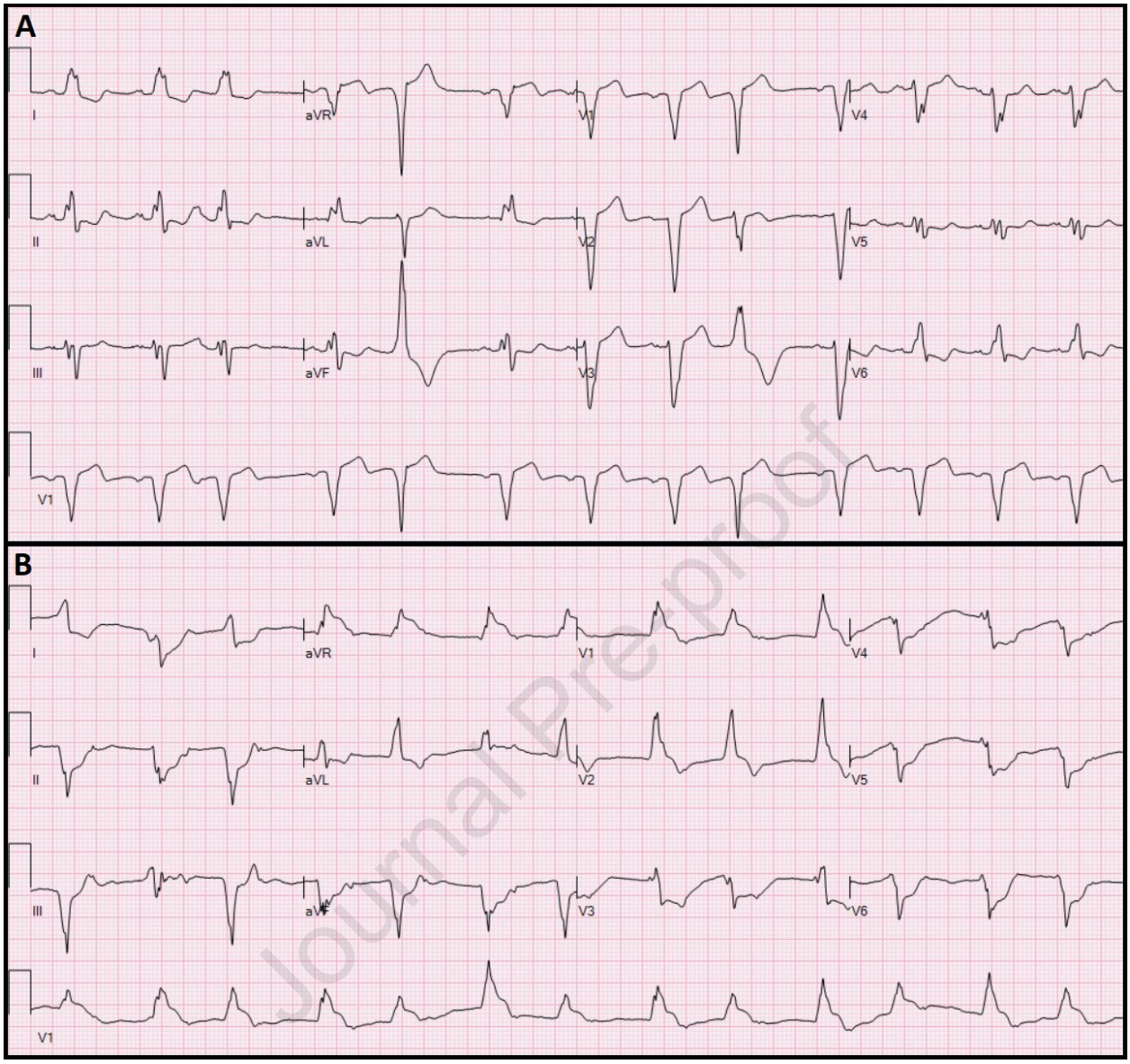

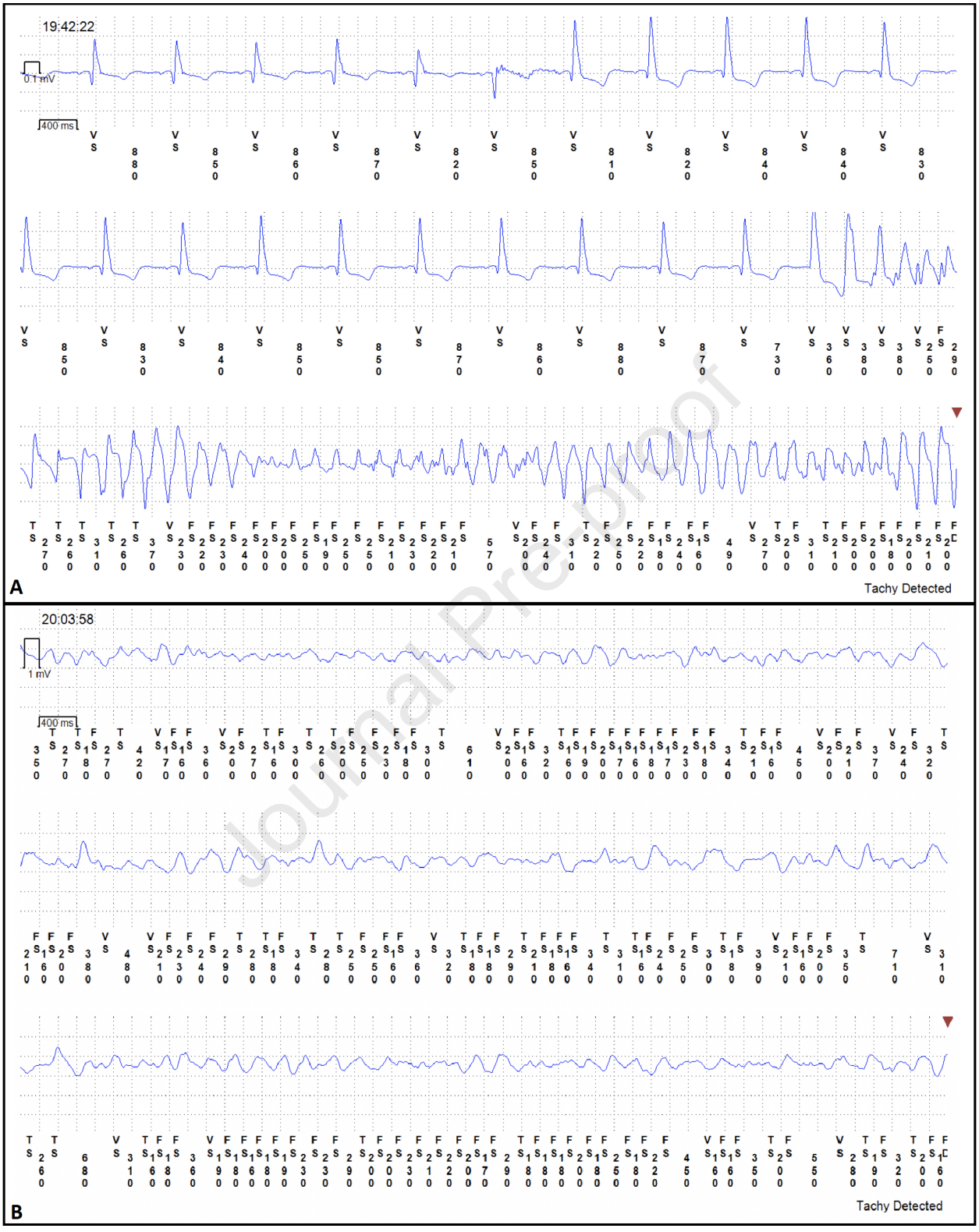

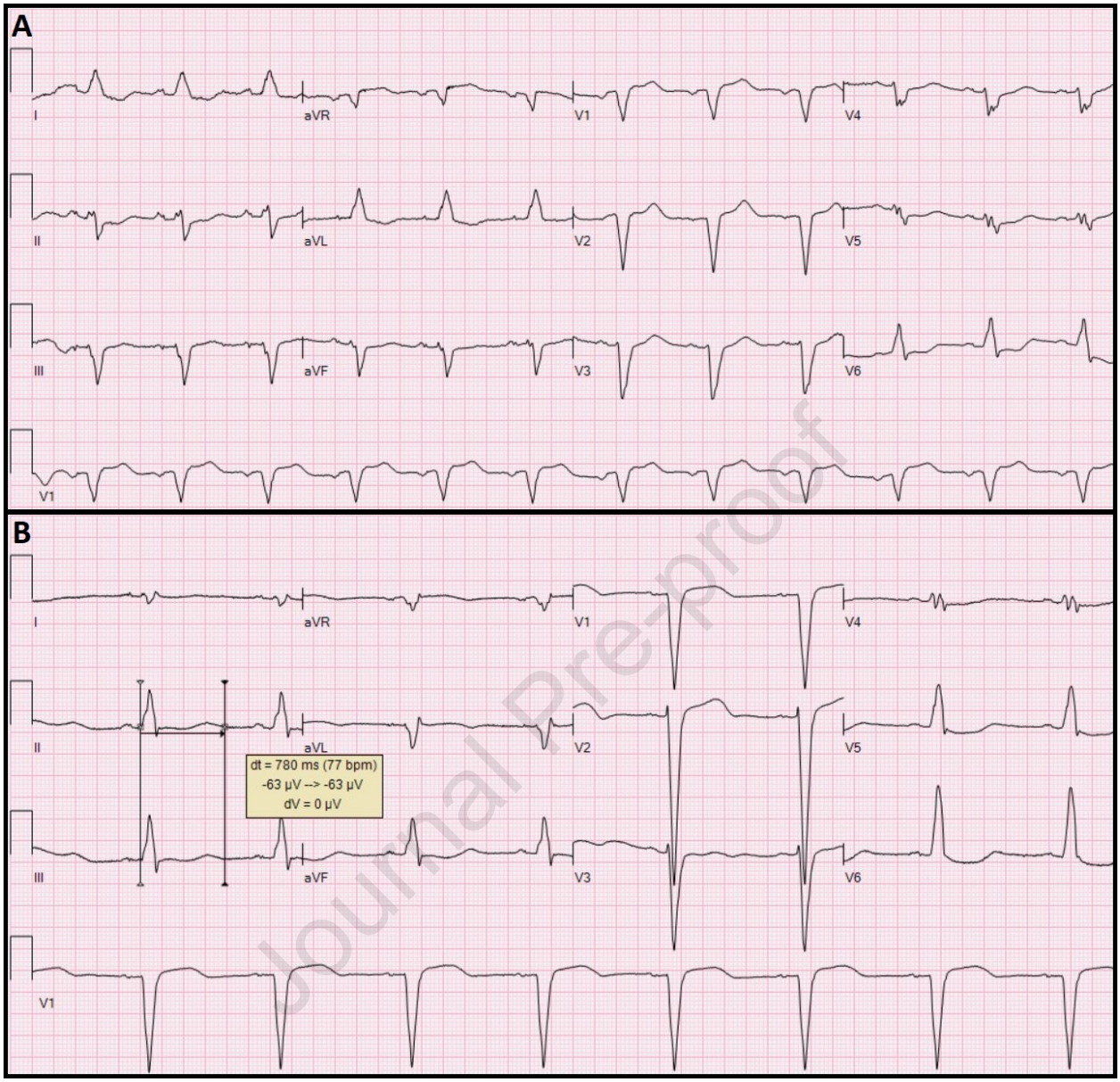

Key Teachings Points

- Vaccination against COVID-19 reduces the incidence of severe illness, hospitalization, and death due to the virus and is associated with a low risk of adverse events.
- COVID-19 infection can cause QT prolongation attributed to excessive inflammation modulating potassium and calcium channels.
- We propose that an excessive immune response following vaccination for COVID-19 may lead to Torsades de Pointes via a similar mechanism to infection in a susceptible individual.